


Day : Monday
Date: 2/19/2007

Time: 15:47:34

 **PALM INTRANET**

Inventor Information for 10/781318

| | | |
|--|-------------|----------------------|
| Inventor Name | City | State/Country |
| CONKLIN, DANIEL J.  | LOUISVILLE | KENTUCKY |

| | | | | | |
|-------------------|-----------------|----------------------|------------------------|--------------------------|------------------|
| Appln Info | Contents | Petition Info | Atty/Agent Info | Continuity/Reexam | Foreign C |
|-------------------|-----------------|----------------------|------------------------|--------------------------|------------------|

Search Another: Application# or Patent#

PCT / / or PG PUBS #

Attorney Docket #

Bar Code #

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Back to [PALM](#) | [ASSIGNMENT](#) | [OASIS](#) | [Home page](#)

EAST Search History

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|-------|-------|--|--------------------------------|------------------|---------|------------------|
| S1 | 63270 | (methylamine or benzylamine or monobenzylamine or aminotoluene or phenylmethanamine or aminomethane or carbinamine or monomethylamine) | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 14:52 |
| S2 | 2667 | S1 and ((vasodilation or vasorelaxation or vaso?) or (blood adj vessel)) | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:22 |
| S3 | 2666 | S1 and ((vasodilation or vasorelaxation) or (blood adj vessel)) | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 14:53 |
| S4 | 28 | S1 and (ssao or (semicarbazide adj sensitive)) | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:20 |
| S5 | 1009 | S3 and (hypertension or (high adj blood)) | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 14:57 |
| S6 | 533 | S3 and (hypertension or (high adj blood)) | USPAT | OR | OFF | 2007/02/19 14:57 |
| S7 | 56 | (ssao or (semicarbazide adj sensitive)) | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:00 |
| S8 | 65397 | ((vasodilation or vasorelaxation or vaso?) or (blood adj vessel)) | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:20 |
| S9 | 4 | S8 and (ssao or (semicarbazide adj sensitive)) | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:20 |
| S10 | 2666 | S1 and ((vasodilation or vasorelaxation) or (blood adj vessel)) | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:22 |
| S11 | 1828 | S10 and (blood adj vessel) | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:23 |
| S12 | 1 | S11 and (vasodilat? or vasorelaxat?) | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:23 |
| S13 | 396 | S11 and implant | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:30 |
| S14 | 13279 | method same (blood adj vessel) | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:31 |
| S15 | 265 | S14 and S1 | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:35 |

EAST Search History

| | | | | | | |
|-----|-------|---|--------------------------------|----|-----|------------------|
| S16 | 2 | S15 and ris | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:32 |
| S17 | 1300 | S14 and (tris adj aminomethane or tris) | US-PGPUB; USPAT | OR | OFF | 2007/02/19 15:32 |
| S18 | 8771 | tris and preserv? | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:35 |
| S19 | 737 | S18 and (blood adj vessel) | US-PGPUB; USPAT; DERWENT | OR | OFF | 2007/02/19 15:35 |
| S20 | 737 | S18 and (blood adj vessel) | US-PGPUB; USPAT | OR | OFF | 2007/02/19 15:36 |
| S21 | 195 | S18 and (blood adj vessel) | USPAT | OR | OFF | 2007/02/19 15:41 |
| S22 | 4 | S21 and millimolar | USPAT | OR | OFF | 2007/02/19 15:38 |
| S23 | 83772 | implantation | USPAT | OR | OFF | 2007/02/19 15:41 |
| S24 | 62 | S21 and S23 | USPAT | OR | OFF | 2007/02/19 15:43 |
| S25 | 1218 | S1 and S23 | USPAT | OR | OFF | 2007/02/19 15:43 |
| S26 | 942 | S25 and (blood adj vessel or artery or tissue) | USPAT | OR | OFF | 2007/02/19 15:44 |

(FILE 'HOME' ENTERED AT 13:47:44 ON 19 FEB 2007)

FILE 'REGISTRY' ENTERED AT 13:50:54 ON 19 FEB 2007

L1 STRUCTURE UPLOADED
L2 130403 S SSS L1 FULL

FILE 'CAPLUS' ENTERED AT 13:56:13 ON 19 FEB 2007

E DILATION+ALL/CT
E VASODILATION+ALL/CT
L3 14 S L2 AND (DILATION OR EXAPANSION OR VASODILATION OR BLOOD VESSE
L4 14 FOCUS L3 1-
L5 178 S L2 AND METHYLAMINE

FILE 'CAPLUS' ENTERED AT 14:03:08 ON 19 FEB 2007

L6 0 S L5 AND (VASODILATION OR VASORELAXATION OR VASODILATE)
L7 STRUCTURE UPLOADED
S L7

FILE 'REGISTRY' ENTERED AT 14:08:34 ON 19 FEB 2007

L8 31447 S L7 SSS FULL

FILE 'CAPLUS' ENTERED AT 14:09:07 ON 19 FEB 2007

L9 4597 S L8 SSS FULL

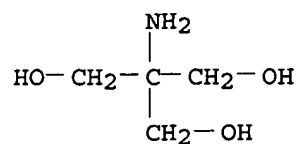
FILE 'CAPLUS' ENTERED AT 14:09:38 ON 19 FEB 2007

FILE 'CAPLUS, USPATFULL' ENTERED AT 14:09:46 ON 19 FEB 2007

L10 5176 S L8
L11 37 S L10 AND (DILATION OR EXAPANSION OR VASODILATION OR BLOOD VESS
L12 2 S L10 AND (SEMICARBAZIDE SENSITIVE AMINE OXIDASE OR SSAO OR SSA
L13 2 DUP REM L12 (0 DUPLICATES REMOVED)
L14 36 DUP REM L11 (1 DUPLICATE REMOVED)
L15 38 S L13 OR L14
L16 38 DUP REM L15 (0 DUPLICATES REMOVED)
L17 38 FOCUS L16 1-
L18 0 S CONKLIN/INV
L19 0 S CONKLIN/INV.
L20 0 S CONKLIN AND L17
L21 788 S CONKLIN
L22 4 S L21 AND (SEMICARBAZIDE SENSITIVE AMINE OXIDASE OR SSAO OR SSA
L23 4 DUP REM L22 (0 DUPLICATES REMOVED)
L24 330 S L10 AND (BLOOD VESSEL OR ARTERY)
L25 216 S L10 AND (BLOOD VESSEL)
L26 59 S L25 AND (HYPERTENSION OR HIGH BLOOD PRESSURE OR VASOSPASM OR
L27 59 FOCUS L26 1-
L28 10 S L25 AND (PD <=2004)
L29 10 FOCUS L28 1-
L30 82 S (BLOOD VESSEL) AND (SEMICARBAZIDE SENSITIVE AMINE OXIDASE OR
L31 82 S L30 AND ?AMINE
L32 36 S L31 AND (SUBSTRATE)
L33 26 S L32 AND PD <+2004
L34 29 S L32 AND PD <=2004

=>

L3 ANSWER 52 OF 52 REGISTRY COPYRIGHT 2007 ACS on STN
 RN 77-86-1 REGISTRY
 ED Entered STN: 16 Nov 1984
 CN 1,3-Propanediol, 2-amino-2-(hydroxymethyl)- (8CI, 9CI) (CA INDEX NAME)
 OTHER NAMES:
 CN 2-Amino-1,3-dihydroxy-2-(hydroxymethyl)propane
 CN 2-Amino-2-(hydroxymethyl)propane-1,3-diol
 CN 2-Amino-2-hydroxymethylpropan-1,3-diol
 CN 2-Amino-2-methylol-1,3-propanediol
 CN Addex-Tham
 CN Aminotri(hydroxymethyl)methane
 CN Aminotrimethylolmethane
 CN Aminotris(hydroxymethyl)methane
 CN Methanamine, 1,1,1-tris(hydroxymethyl)-
 CN NSC 103026
 CN NSC 6365
 CN NSC 65434
 CN Pehanorm
 CN Sarkosyl
 CN Talatrol
 CN TAM
 CN TAM (buffering agent)
 CN THAM
 CN Tri Amino
 CN Tri(hydroxymethyl)methylamine
 CN Trigmo base
 CN Triladyl
 CN Trimethylolaminomethane
 CN Tris
 CN Tris (buffering agent)
 CN Tris Amino
 CN Tris Amino Crystal
 CN Tris base
 CN Tris buffer
 CN Tris(hydroxymethyl)aminomethane
 CN Tris(hydroxymethyl)methanamine
 CN Tris(hydroxymethyl)methylamine
 CN Tris(methylolamino)methane
 CN Tris-steril
 CN Trisamin
 CN Trisamine
 CN Trisaminol
 CN Trispuffer
 CN Trizma
 CN Trometamol
 CN Trometamole
 CN Tromethamine
 CN Tromethane
 CN Tromethanmin
 CN Tutofusin tris
 CN [2-Hydroxy-1,1-bis(hydroxymethyl)ethyl]amine
 DR 857365-23-2, 25149-07-9, 119320-15-9, 68755-45-3, 83147-39-1, 108195-86-4
 MF C4 H11 N O3
 CI COM
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*,
 BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS,
 CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DRUGU,
 EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*,
 MSDS-OHS, PATDPASPC, PIRA, PROMT, PS, RTECS*, SPECINFO, TOXCENTER, USAN,
 USPAT2, USPATFULL, VETU
 (*File contains numerically searchable property data)
 Other Sources: DSL**, EINECS**, TSCA**, WHO
 (**Enter CHEMLIST File for up-to-date regulatory information)



****PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT****

6037 REFERENCES IN FILE CA (1907 TO DATE)
 371 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 6088 REFERENCES IN FILE CAPLUS (1907 TO DATE)
 71 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=>

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2007 ACS on STN
RN 3400-38-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN Methanol, (methylamino)- (7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN (Methylamino)methanol
CN Hydroxymethylaminomethane
MF C2 H7 N O
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CIN, IFICDB,
IFIPAT, IFIUDB, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

HO-CH₂-NH-CH₃

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

38 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
38 REFERENCES IN FILE CAPLUS (1907 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L3 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2007 ACS on STN
 RN 100-46-9 REGISTRY
 ED Entered STN: 16 Nov 1984
 CN Benzenemethanamine (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Benzylamine (8CI)
 OTHER NAMES:
 CN (Aminomethyl)benzene
 CN (Phenylmethyl)amine
 CN α -Aminotoluene
 CN ω -Aminotoluene
 CN 1-Phenylmethanamine
 CN Monobenzylamine
 CN N-Benzylamine
 CN NSC 8046
 CN Phenylmethanamine
 DR 857483-23-9, 858831-93-3
 MF C7 H9 N
 CI COM
 LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHM, CSNB, DDFU, DETHERM*, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PIRA, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USPAT2, USPATFULL
 (*File contains numerically searchable property data)
 Other Sources: DSL**, EINECS**, TSCA**
 (**Enter CHEMLIST File for up-to-date regulatory information)

H₂N-CH₂-Ph

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

19455 REFERENCES IN FILE CA (1907 TO DATE)
 623 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 19507 REFERENCES IN FILE CAPLUS (1907 TO DATE)
 6 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L3 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2007 ACS on STN
 RN 74-89-5 REGISTRY
 ED Entered STN: 16 Nov 1984
 CN Methanamine (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Methylamine (8CI)
 OTHER NAMES:
 CN Aminomethane
 CN Carbinamine
 CN MMA
 CN Monomethylamine
 DR 119775-09-6, 85404-17-7, 42939-70-8
 MF C H5 N
 CI COM
 LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHM, CSNB, DDFU, DETHERM*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PIRA, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USPAT2, USPATFULL, VETU, VTB
 (*File contains numerically searchable property data)

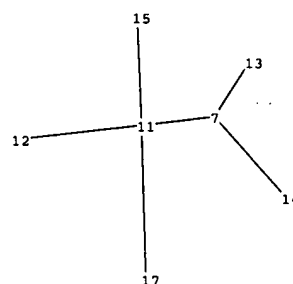
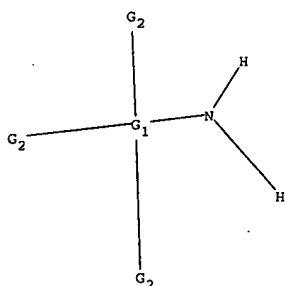
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

H₃C-NH₂

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

18709 REFERENCES IN FILE CA (1907 TO DATE)
1059 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
18741 REFERENCES IN FILE CAPLUS (1907 TO DATE)
13 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=>



chain nodes :

7 11 12 13 14 15 17

ring nodes :

1 2 3 4 5 6

chain bonds :

7-11 7-13 7-14 11-12 11-15 11-17

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-11 11-12 11-15 11-17

exact bonds :

7-13 7-14

G1: Ak,Cb,Hy,[*1]

G2: H,OH,COOH,NH2

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 17:CLASS

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 13:47:44 ON 19 FEB 2007

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

1.05

1.05

FILE 'REGISTRY' ENTERED AT 13:50:54 ON 19 FEB 2007

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STRUCTURE FILE UPDATES: 18 FEB 2007 HIGHEST RN 921759-52-6

DICTIONARY FILE UPDATES: 18 FEB 2007 HIGHEST RN 921759-52-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\methylanine.str

L1 STRUCTURE UPLOADED

=> s sss l1 full

FULL SEARCH INITIATED 13:51:11 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 22758525 TO ITERATE

| | | |
|----------------|--------------------|----------------|
| 1.1% PROCESSED | 260919 ITERATIONS | 31990 ANSWERS |
| 2.0% PROCESSED | 457784 ITERATIONS | 55295 ANSWERS |
| 3.6% PROCESSED | 819629 ITERATIONS | 110305 ANSWERS |
| 4.0% PROCESSED | 907287 ITERATIONS | 121940 ANSWERS |
| 4.2% PROCESSED | 949598 ITERATIONS | 124905 ANSWERS |
| 4.4% PROCESSED | 1000000 ITERATIONS | 130403 ANSWERS |

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.01.32

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**

BATCH **INCOMPLETE**
PROJECTED ITERATIONS: 22758525 TO 22758525
PROJECTED ANSWERS: 2962697 TO 2972861

L2 130403 SEA SSS FUL L1

=> file caplus

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 175.70 | 176.75 |

FILE 'CAPLUS' ENTERED AT 13:56:13 ON 19 FEB 2007
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FILE COVERS 1907 - 19 Feb 2007 VOL 146 ISS 9
FILE LAST UPDATED: 18 Feb 2007 (20070218/ED)

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<http://www.cas.org/infopolicy.html>

=> s l2 and (dilation or exapansion or vasodilation or blood vessel dilation or vascular dilation or vascular relaxation or vasorelaxation)

12360 L2
19502 DILATION
632 DILATIONS
19806 DILATION
(DILATION OR DILATIONS)
5 EXAPANSION
20428 VASODILATION
179 VASODILATIONS
20471 VASODILATION
(VASODILATION OR VASODILATIONS)
1289271 BLOOD
1248 BLOODS
1289412 BLOOD
(BLOOD OR BLOODS)
230988 VESSEL
90275 VESSELS
283577 VESSEL
(VESSEL OR VESSELS)
19502 DILATION
632 DILATIONS
19806 DILATION
(DILATION OR DILATIONS)
2366 BLOOD VESSEL DILATION
(BLOOD (W) VESSEL (W) DILATION)
166492 VASCULAR
6 VASCULARS
166496 VASCULAR

(VASCULAR OR VASCULARS)
 19502 DILATION
 632 DILATIONS
 19806 DILATION
 (DILATION OR DILATIONS)
 170 VASCULAR DILATION
 (VASCULAR(W) DILATION)
 166492 VASCULAR
 6 VASCULARS
 166496 VASCULAR
 (VASCULAR OR VASCULARS)
 251649 RELAXATION
 12732 RELAXATIONS
 254997 RELAXATION
 (RELAXATION OR RELAXATIONS)
 926 VASCULAR RELAXATION
 (VASCULAR(W) RELAXATION)
 2597 VASORELAXATION
 85 VASORELAXATIONS
 2625 VASORELAXATION
 (VASORELAXATION OR VASORELAXATIONS)
 L3 14 L2 AND (DILATION OR EXPANSION OR VASODILATION OR BLOOD VESSEL
 DILATION OR VASCULAR DILATION OR VASCULAR RELAXATION OR VASORELA
 XATION)

=> focus

PROCESSING COMPLETED FOR L3

L4 14 FOCUS L3 1-

=> d ibib abs 1-14 hitstr

L4 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1173484 CAPLUS

DOCUMENT NUMBER: 145:489283

TITLE: N-Acylpiperidines and related compounds as
 CGRP-antagonists, methods for preparing them,
 pharmaceutical compositions and their use as
 pharmaceutical compositions

INVENTOR(S): Mueller, Stephan Georg; Rudolf, Klaus; Lustenberger,
 Philipp; Stenkamp, Dirk; Santagostino, Marco; Paleari,
 Fabio; Schaenzle, Gerhard; Arndt, Kirsten; Doods,
 Henri

PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany

SOURCE: U.S. Pat. Appl. Publ., 156pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| US 2006252931 | A1 | 20061109 | US 2006-277177 | 20060322 |
| WO 2005092880 | A1 | 20051006 | WO 2005-EP3094 | 20050323 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, | | | |

L34 ANSWER 1 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:672498 CAPLUS

DOCUMENT NUMBER: 141:259314

TITLE: A peptide inhibitor of vascular adhesion protein-1 (VAP-1) blocks leukocyte-endothelium interactions under shear stress

AUTHOR(S): Yegutkin, Gennady G.; Salminen, Tiina; Koskinen, Kaisa; Kurtis, Christian; McPherson, Michael J.; Jalkanen, Sirpa; Salmi, Marko

CORPORATE SOURCE: MediCity Research Laboratory, Turku University and National Public Health Institute, Turku, Finland

SOURCE: European Journal of Immunology (2004), 34(8), 2276-2285

CODEN: EJIMAF; ISSN: 0014-2980

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Vascular adhesion protein-1 (VAP-1) is an endothelial adhesion mol. mediating leukocyte interactions with blood vessels during leukocyte extravasation. Molecularly VAP-1 is a cell-surface-expressed ecto-enzyme belonging to the group of semicarbazide-sensitive amine oxidases (SSAO; EC 2.4.6.3), which deaminate primary amines. Here the authors asked whether peptides displaying a suitable free amine group could be a substrate or inhibitor of SSAO and thus regulate VAP-1-mediated leukocyte adhesion. On the basis of a mol. model of VAP-1, the authors designed synthetic peptides that fit to the substrate channel of VAP-1. One of these lysine-containing peptides effectively inhibits VAP-1-dependent lymphocyte rolling and firm adhesion to primary endothelial cells under physiol. relevant shear conditions. The same peptide inhibits the SSAO activity of endothelial and recombinant VAP-1 in a selective and long-lasting manner. The authors also show that all enzymically active VAP-1 is displayed on the cell surface. The authors' results suggest that, in addition to soluble amines, specific cell-surface-bound mols. containing free NH₂ groups in a suitable position may modulate the enzymic activity of SSAO. Moreover, the inhibitory peptide diminishes leukocyte interactions with endothelial cells under conditions of shear, and thus it may be useful to treat inflammatory conditions.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:383251 CAPLUS

DOCUMENT NUMBER: 140:417085

TITLE: Semicarbazide-sensitive amine oxidase: Current status and perspectives

AUTHOR(S): Matyus, P.; Dajka-Halasz, B.; Foeldi, A.; Haider, N.; Barlocco, D.; Magyar, K.

CORPORATE SOURCE: Department of Organic Chemistry, Semmelweis University, Budapest, Hung.

SOURCE: Current Medicinal Chemistry (2004), 11(10), 1285-1298

CODEN: CMCHE7; ISSN: 0929-8673

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Semicarbazide-sensitive amine-oxidase (SSAO) is present in various human tissues and in plasma. Oxidative deamination of short-chain aliphatic amines is catalyzed by this enzyme to afford the corresponding aldehydes, ammonia and hydrogen peroxide. Methylamine and aminoacetone have been

recognized to be physiol. substrates for SSAO. There are several pathol. states where increased serum SSAO activity have been found, such as diabetes mellitus, congestive heart failure, multiple types of cerebral infarction, uremia, and hepatic cirrhosis. The role of SSAO in pathophysiol. of diabetes has been most extensively investigated. The elevated formation of the potentially cytotoxic products of the enzyme may contribute to the endothelial injury of blood vessels, resulting in the early development of severe atherosclerosis; it may also contribute to the pathogenesis of diabetic angiopathy. It is now suggested that SSAO inhibitors may prevent the development of atherosclerosis and diabetic complications as well. Inhibitors can be conveniently subdivided into the main groups of hydrazine derivs., arylalkylamines, propenyl- and propargylamines, oxazolidinones, and haloalkylamines. Of them, aryl(alkyl)hydrazines, and 3-halo-2-phenylallyl amines are generally very strong SSAO inhibitors. Most of these inhibitors of SSAO have been originally developed for other purposes, or they are simple chemical reagents with highly reactive structural element(s); these compds. have not been able to fulfil all criteria of high potency, selectivity, and acceptable toxicity. New potent compds. with selectivity and low toxicity are needed, which may prove useful tools for understanding the roles and function of SSAO, or they may even be valuable substances for treatment of various diseases.

REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:308809 CAPLUS

DOCUMENT NUMBER: 140:389683

TITLE: Semicarbazide-sensitive amine oxidase overexpression has dual consequences: insulin mimicry and diabetes-like complications

AUTHOR(S): Stolen, Craig M.; Madanat, Rami; Marti, Luc; Kari, Seppo; Yegutkin, Gennady G.; Sariola, Hannu; Zorzano, Antonio; Jalkanen, Sirpa

CORPORATE SOURCE: MediCity Res. Lab., Univ. of Turku and Natl. Public Health Inst., Turku, 20520, Finland

SOURCE: FASEB Journal (2004), 18(6), 702-704, 10.1096/fj.03-0562fje
CODEN: FAJOEC; ISSN: 0892-6638

PUBLISHER: Federation of American Societies for Experimental Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Semicarbazide-sensitive amine oxidases (SSAO) are copper-containing enzymes that oxidatively deaminate primary amines to produce hydrogen peroxide, ammonium, and specific aldehydes. Vascular adhesion protein-1 (VAP-1) is a cell surface and soluble mol. that possesses SSAO activity. VAP-1 protein, SSAO activity, and SSAO reaction products are elevated in the serum of patients with diabetes, congestive heart failure, and specific inflammatory liver diseases. By expressing human VAP-1/SSAO on mouse endothelial cells and subsequently in the serum, and by chronically treating the transgenic mice for 15 mo with a high-fat diet and a physiol. substrate for SSAO, methylamine, the in vivo roles of SSAO were assessed. The VAP-1 transgene increased the mouse body mass index and s.c. abdominal fat pad wts. in a manner independent of food consumption. The transgene together with increased SSAO substrate availability enhanced glucose uptake in an SSAO-dependent manner. The increased SSAO activity also led to diabetes-like complications, including advanced glycation end product formation, elevated blood pressure, altered atherosclerosis progression, and nephropathy. These

findings suggest that, although manipulation of VAP-1/SSAO has potential to serve as a therapeutic treatment in insulin-resistant conditions, care must be taken to fully understand its impact on obesity and vascular damage.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs 4-29

L34 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:780531 CAPLUS

DOCUMENT NUMBER: 139:394456

TITLE: Serum semicarbazide-sensitive amine oxidase activity in patients with retinopathy in type 2 diabetes mellitus

AUTHOR(S): Dura, E.; Meszaros, Zs.; Salacz, Gy.; Magyar, K.; Romics, L.; Karadi, I.

CORPORATE SOURCE: 2nd Department of Ophthalmology, Semmelweis University, Budapest, Hung.

SOURCE: Diabetes Research (2001), Volume Date 2000-2001, 35(4), 127-141

CODEN: DIREEM; ISSN: 0265-5985

PUBLISHER: Teviot-Kimpton Publications

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study aimed to examine the association between serum semicarbazide-sensitive amine oxidase (SSAO) activity and the severity of retinopathy in Type 2 diabetic patients. Recent data suggest that this amine oxidase enzyme may play a role in vascular endothelial damage through conversion of certain endogenous monoamines, like methylamine, into cytotoxic aldehydes, hydrogen peroxide and ammonia. A prospective study was performed on a defined group of Type 2 diabetic patients (n=93) compared to non-diabetic control subjects (n=42). Age at diagnosis, gender, duration of diabetes, presence of systemic hypertension and BMI were recorded. All participants underwent a detailed ophthalmic evaluation, color retinal photog. and laboratory investigations. Besides routine metabolic parameters and renal function characteristics, serum SSAO activity was determined by a radio-enzymic procedure using [¹⁴C]-benzylamine as substrate. SSAO activity (mean±SD) was significantly higher in patients with high-risk proliferative diabetic retinopathy (n=16, 166.96±70.56 pmol.mg-1 protein.hour-1) compared to those without retinopathy (n=42, 119.54±50.49 pmol.mg-1 protein.hour-1). In the total group of Type 2 diabetic patients SSAO activity was significantly elevated compared to nondiabetic controls (n=93, 131.72±53.07 vs. n=42, 89.56±26.89 pmol.mg-1 protein.hour-1). Our results support the hypothesis that elevated SSAO activity may be involved in the pathogenesis of microvascular diabetic late complications, such as retinopathy.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:274108 CAPLUS

DOCUMENT NUMBER: 139:34047

TITLE: Physiological and pathological implications of semicarbazide-sensitive amine oxidase

AUTHOR(S): Yu, Peter H.; Wright, Shannon; Fan, Ellen H.; Lun, Zhao-Rong; Gubisne-Harberle, Diana

CORPORATE SOURCE: Medical Research Building, College of Medicine, Department of Psychiatry, Neuropsychiatry Research

Unit, University of Saskatchewan, Saskatoon, SK, A114, Can.

SOURCE: Biochimica et Biophysica Acta, Proteins and Proteomics (2003), 1647(1-2), 193-199
CODEN: BBAPBW; ISSN: 1570-9639
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Semicarbazide-sensitive amine oxidase (SSAO) catalyzes the deamination of primary amines. Such deamination has been shown capable of regulating glucose transport in adipose cells. It has been independently discovered that the primary structure of vascular adhesion protein-1 (VAP-1) is identical to SSAO. VAP-1 regulates leukocyte migration and is related to inflammation. Increased serum SSAO activities have been found in patients with diabetic mellitus, vascular disorders and Alzheimer's disease. The SSAO-catalyzed deamination of endogenous substrates, i.e., methylamine and aminoacetone, led to production of toxic formaldehyde and methylglyoxal, hydrogen peroxide and ammonia, resp. These highly reactive aldehydes have been shown to initiate protein cross-linkage, exacerbate advanced glycation of proteins and cause endothelial injury. Hydrogen peroxide contributes to oxidative stress. 14C-methylamine is converted to 14C-formaldehyde, which then forms labeled long-lasting protein adduct in rodents. Chronic methylamine treatment increased the excretion of malondialdehyde and microalbuminuria, and enhanced the formation of fatty streaks in C57BL/6 mice fed with an atherogenic diet. Treatment with selective SSAO inhibitor reduces atherogenesis in KKAY diabetic mice fed with high-cholesterol diet. Aminoguanidine, which blocks advanced glycation and reduces nephropathy in animals, is in fact more potent at inhibiting SSAO than its effect on glycation. It suggests that SSAO is involved in vascular disorders under certain pathol. conditions. Although SSAO has been known for several decades, its physiol. and pathol. implications are just beginning to be recognized.

REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:274083 CAPLUS

DOCUMENT NUMBER: 139:34044

TITLE: Plasma semicarbazide-sensitive amine oxidase in human (patho)physiology

AUTHOR(S): Boomsma, Frans; Bhaggoe, Usha M.; van der Houwen, Angelique M. B.; van den Meiracker, Anton H.

CORPORATE SOURCE: Department of Internal Medicine, Erasmus MC, Rotterdam, 3015 GD, Neth.

SOURCE: Biochimica et Biophysica Acta, Proteins and Proteomics (2003), 1647(1-2), 48-54
CODEN: BBAPBW; ISSN: 1570-9639

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with refs. Semicarbazide-sensitive amine oxidases (SSAO) are widely distributed enzymes, with as yet not fully elucidated functions and roles, present in many tissues but also circulating in plasma. The enzyme also functions as an adhesion mol., the vascular adhesion protein-1. In healthy humans, plasma SSAO activity is constant from birth until 16 yr of age, when it drops to lower values, gradually increasing again at advanced ages. When measuring SSAO activity, care should be taken to ensure proper preparation and storage conditions, and it should be realized that quite a few drugs unintentionally are good inhibitors, and sometimes even substrates, of SSAO. Under normal conditions

SSAO activity is constant and inter-individual variation is small. In various pathophysiol. conditions plasma SSAO activities are increased, most notably in diabetes mellitus (both type I and type II), in congestive heart failure and in cirrhotic liver inflammation. In patients with other vascular and inflammatory diseases plasma SSAO is normal, while it is low in children with congenital lung diseases. Interpretation of these changes is speculative, since source and regulation of plasma SSAO are as yet unknown. However, in two situations where the disease-causing process was ended (transplantation, delivery), plasma SSAO returned to normal. Many questions remain to be answered.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:817630 CAPLUS

DOCUMENT NUMBER: 138:268952

TITLE: Semicarbazide-sensitive amine oxidase and extracellular matrix deposition by smooth-muscle cells

AUTHOR(S): Langford, Shannon D.; Trent, Margaret B.; Boor, Paul J.

CORPORATE SOURCE: Wyle Laboratories, Cellular Biotechnology-Flight Definition, NASA Johnson Space Center, Houston, TX, 77058, USA

SOURCE: Cardiovascular Toxicology (2002), 2(2), 141-150

CODEN: CTAOAT; ISSN: 1530-7905

PUBLISHER: Humana Press Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have recently reported in vivo disruption of collagen and elastin architecture within blood vessel walls resulting from the selective inhibition of the enzyme semicarbazide-sensitive amine oxidase (SSAO). This study further investigates the effects of SSAO inhibition on extracellular matrix deposition by smooth-muscle cells (SMCs) cultured from neonatal rat hearts. SMCs were characterized, SSAO activity was measured, and soluble and insol. collagen and elastin in the extracellular matrix (ECM) were quantified. Cultured neonatal rat heart SMC exhibited a monotypic synthetic phenotype that likely represents a myofibroblast. Detectable levels of SSAO activity present throughout 30-d culture peaked at 7-14 d, coinciding with the production of ECM. The addition of enzyme inhibitors and alternate SSAO substrates (benzylamine) produced varied and, in some cases, marked changes in SSAO activity as well as in the composition of mature and soluble matrix components. Similar to our previous in vivo findings, in vitro SSAO inhibition produced aberrations in collagen and elastin deposition by heart SMC. Because changes in SSAO activity are associated with cardiovascular pathol. states, this enzyme may play a protective or modulating role by regulating ECM production during pathol. insult.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:569076 CAPLUS

DOCUMENT NUMBER: 138:35044

TITLE: Enzymic characteristics and physiological roles of mammalian tissue-bound semicarbazide-sensitive amine oxidase

AUTHOR(S): Kinemuchi, Hiroyasu; Kobayashi, Naoyuki; Takahashi, Kazuya; Takayanagi, Kaori; Takahashi, Kaori

CORPORATE SOURCE: Department of Basic Science, School of Science and

Engineering, Ishinomaki Senshu University, Ishinomaki,
986-8580, Japan
SOURCE: Ishinomaki Senshu Daigaku Kenkyu Kiyo (2001
, 12, 67-83
CODEN: ISDKFS; ISSN: 0915-8715
PUBLISHER: Ishinomaki Senshu Daigaku
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. Mammalian tissues contain membrane-bound semicarbazide
-sensitive amine oxidase (SSAO)
which metabolizes the synthetic amine benzylamine
extremely well. The sensitivity of this enzyme to inhibition by
semicarbazide and related compds. indicates that it contains a reactive
carbonyl group(s), as a co-factor, which recently has been identified as
6-hydroxydopa quinone (topa quinone). Many compds. have now been
identified as relatively selective inhibitors to distinguish the
SSAO from e.g. monoamine oxidase, in order to study the
properties of SSAO and its potential role in biogenic and
xenobiotic amine metabolism. We recently developed a potent and
specific suicide-SSAO inhibitor, 2-bromoethylamine.
Using this inhibitor, it is possible to study the role of the enzyme in
various mammalian tissues. The tissue SSAO is membrane-bound,
probably plasmalemmal enzyme, which may metabolize extracellular amines.
There is some evidence that SSAO in the plasmalemma may face
outward to metabolize extracellular amines without any help of the
membrane re-uptake system. Vascular and non-vascular smooth muscle cells
have particularly high SSAO activity, but recently the enzyme
has been found in adipocytes, chondrocytes, odontoblasts, implying a
functional importance not restricted solely to smooth muscle. The
substrate specificity of tissue SSAO shows considerable
species-related variations. For example, some endogenously-occurring
aromatic amines such as tyramine and tryptamine are
oxidized well by tissue-bound SSAO from rat blood
vessels. Inhibition of SSAO activity potentiates
vasoconstrictor actions of these amines in rat vascular preps., although
these amines are poor substrate for human SSAO, thus
complicating attempt to generalize possible physiol. roles in the
mammalian tissues for this enzyme. More recently, the complete primary
sequence of bovine SSAO has been deduced from a bovine liver
cDNA library. This predicted a sequence of 762 amino acids with mol. weight
of 84,750 Da. Recent studies showed that vascular SSAO
metabolizes in vitro and in vivo aliphatic xenobiotic and endogenous amines,
such as allylamine, methylamine and aminoacetone to
the cytotoxic aldehydes and these have been linked to the ability of
diabetic complications.

L34 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:67711 CAPLUS
DOCUMENT NUMBER: 136:260479
TITLE: Semicarbazide-sensitive
amine oxidase in vascular smooth
muscle cells: differentiation-dependent expression and
role in glucose uptake
AUTHOR(S): El Hadri, Khadija; Moldes, Marthe; Mercier, Nathalie;
Andreani, Marise; Pairault, Jacques; Feve, Bruno
CORPORATE SOURCE: Centre de Recherches Biomedical des Cordeliers,
Universite Pierre et Marie Curie, Paris, 75270, Fr.
SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology (
2002), 22(1), 89-94
CODEN: ATVBFA; ISSN: 1079-5642
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cultured vascular smooth muscle cells (VSMCs) derived from rat aortic

media were used to examine semicarbazide-sensitive amine oxidase (SSAO) expression during their differentiation process. In a defined serum-free medium permissive for in vitro VSMC differentiation, there was a large increase in SSAO mRNA and protein levels and in the related enzyme activity during the course of cell culture. This pattern of expression was concomitant with that of some smooth muscle-specific mRNA markers of differentiation. MRNAs in differentiated cultured VSMCs were comparable to those detected in total aorta and media. Pharmacol. properties of SSAO present in VSMCs were similar to enzyme activities previously described in the aortic wall. In this model, we also demonstrated that methylamine, a physiol. substrate of SSAO, activated 2-deoxyglucose transport in a time- and dose-dependent manner. This methylamine effect was reproduced by other SSAO substrates and was prevented by the SSAO inhibitor semicarbazide. It was antagonized in the presence of catalase, suggesting that SSAO-activated glucose transport was mediated through H₂O₂ production. In addition, methylamine promoted glucose transporter 1 accumulation at the cell surface. Thus, we demonstrate for the first time the differentiation-dependent expression of SSAO in VSMCs and its role in the regulation of VSMC glucose uptake.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:915600 CAPLUS

DOCUMENT NUMBER: 136:146909

TITLE: Semicarbazide-sensitive amine oxidase. Its physiological significance

AUTHOR(S): Magyar, K.; Meszdros, Z.; Matyus, P.

CORPORATE SOURCE: IUPAC Commission, Department of Pharmacodynamics, Department of Organic Chemistry, Faculty of Pharmacy, Semmelweis University, Budapest, Hung.

SOURCE: Pure and Applied Chemistry (2001), 73(9), 1393-1400

CODEN: PACHAS; ISSN: 0033-4545

PUBLISHER: International Union of Pure and Applied Chemistry

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Although the existence of plasma- and tissue-bound semicarbazide-sensitive amine oxidases (SSAOs) has been recognized earlier, the physiol. relevance of the enzyme still remains uncertain. Recent data suggest that elevated serum SSAO activity might cause endothelial injury. Formation of cytotoxic metabolites (e.g., formaldehyde) and increased oxidative stress might lead to initiation or progression of atherosclerosis. Significant pos. correlation was found between serum SSAO activity and severity of atherosclerosis, and diabetic macrovascular complications. Effective and selective inhibitors of human SSAO might exert cytoprotective effect on endothelial cells. Compds. having similar structure to mexiletine were synthesized and studied relating to SSAO activity. The reference substrate was MDL-72974A. Unfortunately, our new compds. did not reach the potency of the reference substance using human serum samples. In conclusion, we suppose that vascular and soluble SSAO enzymes might have different inhibitor sensitivity. Further studies are required to determine whether the soluble or vascular isoform of SSAO will be the main therapeutic target in the future.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 11 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:373602 CAPLUS
 DOCUMENT NUMBER: 135:150947
 TITLE: Semicarbazide-sensitive
 amine oxidase catalyzes endothelial
 cell-mediated low density lipoprotein oxidation
 AUTHOR(S): Exner, M.; Hermann, M.; Hofbauer, R.; Kapiotis, S.;
 Quehenberger, P.; Speiser, W.; Held, I.; Gmeiner, B.
 M. K.
 CORPORATE SOURCE: Clinical Institute of Medical and Chemical Laboratory
 Diagnostics, University of Vienna, Vienna, Austria
 SOURCE: Cardiovascular Research (2001), 50(3),
 583-588
 CODEN: CVREAU; ISSN: 0008-6363
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Objective: Deamination products of semicarbazide-
 sensitive amine oxidases (SSAO),
 i.e. aldehydes, superoxide and ammonia have been shown to initiate
 vascular damage. SSAOs are copper-enzymes, present in
 endothelial (EC), smooth muscle cells (SMC) and in blood. Transition
 metals ions (Cu, Fe) mediate the oxidative (atherogenic) modification of
 LDL by SMC and EC. The physiol. source of the active metal ions is still
 under debate. We hypothesize that SSAOs may catalyze LDL oxidation
 by endothelial cells via enzyme-complexed Cu⁺⁺. Methods: EC isolated from
 human umbilical veins and cultured in 35 mm wells in RPMI-1640 medium were
 used as LDL oxidation system. Results: Diamine oxidase (DAO), a
 SSAO which activity is elevated in tissues and sera of diabetic
 patients, catalyzes the oxidation of LDL by EC. In the presence of purified
 DAO (0.07 to 70 U/L) LDL oxidation was increased up to 10-fold as measured by
 thiobarbituric acid reactive substance (TBARS) formation as well as
 apoprotein modification of LDL. Chemical blockage of the SSAO
 substrate binding site did not inhibit the catalytic effect of DAO
 on LDL oxidation. Denaturation of the enzyme did not destroy the ability of
 the preparation to facilitate LDL oxidation by EC. The potential of the
 enzyme to
 catalyze LDL oxidation was not suppressed in the presence of serum. However,
 selective removing of enzyme-copper completely abolished the ability of
 the enzyme to trigger cell-mediated LDL oxidation. Conclusion: DAO, beside
 generating angiopathic deamination products, has the potential to act as a
 pathophysiol. catalyst of LDL atherogenic modification by vascular cells.
 REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:867382 CAPLUS
 DOCUMENT NUMBER: 134:278807
 TITLE: Plasma semicarbazide-sensitive
 amine oxidase (SSAO) is an
 independent prognostic marker for mortality in chronic
 heart failure
 AUTHOR(S): Boomsma, F.; De Kam, P. J.; Tjeerdsma, G.; Van Den
 Meiracker, A. H.; Van Veldhuisen, D. J.
 CORPORATE SOURCE: Department of Internal Medicine, Erasmus university
 Medical Centre Rotterdam, Rotterdam, 3015 GD, Neth.
 SOURCE: European Heart Journal (2000), 21(22),
 1859-1863
 CODEN: EHJODF; ISSN: 0195-668X
 PUBLISHER: W. B. Saunders Co. Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Aims: Exptl. evidence has suggested that semicarbazide-
 sensitive amine oxidase is involved in
 vascular endothelial damage and in the process of atherosclerosis, through

the formation of reactive aldehydes, hydrogen peroxide and ammonia from endogenous substrates. Recent evidence indicates that semicarbazide-sensitive amine oxidase may be identical with the vascular adhesion protein-1. In patients with diabetes mellitus and chronic heart failure the plasma activity is raised relative to the severity of the disease. The prognostic value of plasma semicarbazide-sensitive amine oxidase is not known. Methods and Results: Plasma semicarbazide-sensitive amine oxidase activity was measured at baseline in patients with moderate to severe chronic heart failure who participated in a large European study (PRIME-II). The 372 patients who took part in a pre-defined substudy in The Netherlands were investigated and a survival follow-up (maximum 5.4 yr, mean 3.4 yr) was carried out. Within the follow-up period 195 patients died. Plasma semicarbazide-sensitive amine oxidase was higher at baseline in those who died than in the survivors (653 ± 258 vs. 540 ± 242 mU.l⁻¹, $P < 0.001$). Dividing the patients into two groups according to plasma values above or below the median value of 550 mU.l⁻¹, semicarbazide-sensitive amine oxidase was found to be a prognostic parameter for survival, both in univariate ($P < 0.0001$) and in multivariate ($P = 0.0106$) anal. Semicarbazide-sensitive amine oxidase values > 550 mU.l⁻¹ had a 1.50 (95% CI, 1.10-2.04) times increased risk of death. Conclusion: The finding that plasma semicarbazide-sensitive amine oxidase is an independent prognostic marker for mortality in chronic heart failure supports the concept that an elevated plasma semicarbazide-sensitive amine oxidase level has deleterious effects, possibly due to vascular endothelial damage.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:643258 CAPLUS

DOCUMENT NUMBER: 134:1918

TITLE: Determination of human serum semicarbazide-sensitive amine oxidase activity: a possible clinical marker of atherosclerosis

AUTHOR(S): Meszaros, Z.; Karadi, I.; Csanyi, A.; Szombathy, T.; Romics, L.; Magyar, K.

CORPORATE SOURCE: Department of Pharmacodynamics, Semmelweis University, Budapest, Hung.

SOURCE: European Journal of Drug Metabolism and Pharmacokinetics (1999), 24(4), 299-302
CODEN: EJDPD2; ISSN: 0378-7966

PUBLISHER: Medecine et Hygiene

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Semicarbazide-sensitive amine oxidase (SSAO) is present in the plasma membrane of several human tissues, e.g. vascular smooth muscle cell adipocytes, and is also found in human serum. Some previous studies on cultured endothelial cells indicate that cytotoxic metabolites (e.g. hydrogen peroxide, formaldehyde, acrolein) formed by serum SSAO may cause endothelial injury and subsequently induce atherosclerosis. To investigate the role of this enzyme in the pathogenesis of macrovascular complications in diabetes, a simple and sensitive radiometric procedure was adapted for human serum measurements. Serum SSAO activity of 35 patients with non-insulin dependent diabetes mellitus (NIDDM) and that of 30 controls was determined using [¹⁴C]-benzylamine as substrate. The severity of atherosclerosis was assessed by carotid sonog. Diabetic patients with atherosclerosis exhibited a higher SSAO activity compared to diabetic patients without complications

(212.91±90.54 pmol/mg protein/h vs. 133.17±65.40 pmol/mg protein/h, P <0.04). In diabetic patients without complications, serum SSAO activity was elevated compared to control subjects (133.17 ± 65.40 pmol/mg protein/h vs. 91.79±31.70 pmol/mg protein/h, P<0.01). These results suggest that determination of human serum SSAO activity might be a useful marker in the prognostic evaluation of diabetic angiopathy and atherosclerosis.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:70880 CAPLUS

DOCUMENT NUMBER: 132:247815

TITLE: Presence of SSAO in human and bovine meninges and microvessels

AUTHOR(S): Castillo, V.; Lizcano, J. M.; Unzeta, M.

CORPORATE SOURCE: Department de Bioquímica i Biologia Molecular, Facultat de Medicina, Universitat Autònoma de Barcelona, Bellaterra, Spain

SOURCE: Neurobiology (Budapest) (1999), 7(3), 263-272

CODEN: NROBEZ; ISSN: 1216-8068

PUBLISHER: Akademiai Kiado

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In spite of the fact that semicarbazide-sensitive amine oxidase (SSAO, EC 1.4.3.6) is widely distributed in almost all tissues, specially in vascularized ones, its presence in brain microvessels is still controversy. Our results resolve this question showing that both human and bovine cerebrovascular tissues do contain the SSAO enzyme. This was achieved biochem., using benzylamine and methylamine as substrates, and by immunoblot anal., using polyclonal antibodies anti-SSAO that recognized a 100 kDa single band in tissue homogenates.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 15 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:182214 CAPLUS

DOCUMENT NUMBER: 131:17308

TITLE: Developmental Vasculotoxicity Associated with Inhibition of Semicarbazide-Sensitive Amine Oxidase

AUTHOR(S): Langford, S. D.; Trent, M. B.; Balakumaran, A.; Boor, P. J.

CORPORATE SOURCE: Department of Pathology, University of Texas Medical Branch, Galveston, TX, 77555-0609, USA

SOURCE: Toxicology and Applied Pharmacology (1999), 155(3), 237-244

CODEN: TXAPA9; ISSN: 0041-008X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The endogenous substrate(s) and physiol. function(s) of semicarbazide-sensitive amine oxidase (SSAO), a group of enzymes exhibiting highest activity in vascular smooth muscle cells of the mammalian aortic wall, remain undetd. This study examines the pathophysiol. effects in the thoracic aortic wall resulting from specific in vivo SSAO inhibition. Weanling Sprague-Dawley rats were treated acutely or chronically with either semicarbazide hydrochloride or the allylamine derivs. MDL-72274 or MDL-72145 (Marion Merrell Dow Research Institute, Cincinnati, OH). Treatment with these compds. produced acute (6 and 24 h) and chronic (21

100-46-9
74-89-5

day) lowering of SSAO activity in aorta and lung with little effect on the activity of the vital matrix-forming enzyme, lysyl oxidase, in aortas of chronically treated animals. Chronic SSAO inhibition produced lesions consisting of striking disorganization of elastin architecture within the aortic media accompanied by degenerative medial changes and metaplastic changes in vascular smooth muscle cells. No significant difference in the total weight of dry, lipid-extracted aortic elastin and collagen components were observed between chronically SSAO inhibited and control animals. However, the amount of mature elastin was lowered and mature collagen was raised in the aortas of animals treated chronically with semicarbazide. Descending thoracic aortic rings isolated from chronically SSAO-inhibited animals had larger cross-sectional diam. (i.e., exhibited dilation) when compared to corresponding rings from control animals. This study demonstrates that developmental toxicity, characterized by striking vascular lesions and dilated thoracic aortas, can result from specific in vivo SSAO inhibition, suggesting a role for SSAO in connective tissue matrix development and maintenance, and specifically in the development of normal elastin. (c) 1999 Academic Press.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 16 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:36683 CAPLUS

DOCUMENT NUMBER: 130:221497

TITLE: Elevated serum semicarbazide-sensitive amine oxidase activity in non-insulin-dependent diabetes mellitus: correlation with body mass index and serum triglyceride

AUTHOR(S): Meszaros, Zsuzsa; Szombathy, Tamas; Raimondi, Laura; Karadi, Istvan; Romics, Laszlo; Magyar, Kalman

CORPORATE SOURCE: Department of Pharmacodynamics and Third Department of Medicine, Semmelweis University of Medicine, Budapest, Hung.

SOURCE: Metabolism, Clinical and Experimental (1999), 48(1), 113-117

CODEN: META AJ; ISSN: 0026-0495

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Previous clin. studies reported elevated semicarbazide-sensitive amine oxidase (SSAO) activity in insulin-dependent diabetes mellitus (IDDM), but there are not sufficient data about SSAO in non-insulin-dependent diabetes mellitus (NIDDM). The present study was conducted to investigate serum SSAO activity in NIDDM patients compared with nondiabetic and IDDM patients. Serum SSAO activity in 61 patients with diabetes (n = 34 NIDDM and n = 27 IDDM) and 36 controls was determined using 14C-benzylamine as a substrate. NIDDM and IDDM patients exhibited higher SSAO activity compared with controls ([mean \pm SD] NIDDM, 164.60 \pm 69.43 pmol/mg protein/h, P < .0001; IDDM, 143.91 \pm 72.45 pmol/mg protein/h, P < .002; control, 91.46 \pm 28.11 pmol/mg protein/h). There was a significant pos. correlation between serum SSAO activity and the body mass index (BMI), body weight, HbA1c, fasting plasma glucose, and triglycerides. Within the control group, SSAO correlated with total cholesterol levels. The progression and severity of diabetic complications such as angiopathy may be exacerbated by cytotoxic metabolites (eg, formaldehyde and hydrogen peroxide) formed by SSAO. These results reveal the possibility that elevated serum SSAO activity in association with obesity and hyperlipidemia may be a cardiovascular risk factor in diabetes mellitus.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:330056 CAPLUS
DOCUMENT NUMBER: 129:120408
TITLE: Properties and functions of tissue-bound
semicarbazide-sensitive
amine oxidases in isolated cell
preparations and cell cultures
AUTHOR(S): Lyles, G. A.; Pino, R.
CORPORATE SOURCE: Department of Pharmacology and Clinical Pharmacology,
Ninewells Hospital and Medical School, University of
Dundee, Dundee, UK
SOURCE: Journal of Neural Transmission, Supplement (
1998), 52(MAO - The Mother of all Amine
Oxidases), 239-250
CODEN: JNTSD4; ISSN: 0303-6995
PUBLISHER: Springer-Verlag Wien
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 36 refs. The demonstration of semicarbazide-sensitive amine oxidase (SSAO) activity in some freshly-dispersed cell preps. and in particular types of cells grown in culture provides increasing opportunities for investigating the importance of SSAO in various aspects of cellular function. Assays of benzylamine and methylamine metabolism in homogenates of cultured cells have established clearly that SSAO is expressed in rat and pig vascular (aortic) smooth muscle cells, as well as in rat non-vascular (anococcygeus, trachea) smooth muscle, brown and white adipocytes. However, to date little or no SSAO activity has been detected in cultures of human vascular smooth muscle cells grown from blood vessels (e.g. umbilical artery) known to contain the enzyme, and the reason for this is not yet apparent. However, those cell cultures expressing SSAO are offering useful exptl. models for studying biochem. and toxicol. consequences upon cellular function which may result from the metabolism of various aromatic and aliphatic amines suggested to be possible physiol. and xenobiotic substrates of the enzyme.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:330052 CAPLUS
DOCUMENT NUMBER: 129:107258
TITLE: Deamination of methylamine and angiopathy;
toxicity of formaldehyde, oxidative stress and
relevance to protein glycooxidation in diabetes
AUTHOR(S): Yu, P. H.
CORPORATE SOURCE: Neuropsychiatry Research Unit, College of Medicine,
University of Saskatchewan, Saskatoon, SK, Can.
SOURCE: Journal of Neural Transmission, Supplement (
1998), 52(MAO - The Mother of all Amine
Oxidases), 201-216
CODEN: JNTSD4; ISSN: 0303-6995
PUBLISHER: Springer-Verlag Wien
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 107 refs. Semicarbazide-sensitive amine oxidase (SSAO) is located in the vascular smooth muscles, retina, kidney and the cartilage tissues, and it circulates in the blood. The enzyme activity has been significantly increased in blood and tissues in diabetic patients and animals. Methylamine and aminoacetone are endogenous substrates for SSAO. The deaminated products are formaldehyde and methylglyoxal resp., as well as H2O2 and ammonia, which are all

potentially cytotoxic. Formaldehyde and methylglyoxal are cytotoxic towards endothelial cells. Excessive SSAO-mediated deamination may directly initiate endothelial injury and plaque formation, increase oxidative stress, which can potentiate oxidative glycation, and/or LDL oxidation and damage vascular systems. Formaldehyde is also capable of exacerbating advanced glycation, and thus increase the complexity of protein crosslinking. Uncontrolled SSAO-mediated deamination may be involved in the acceleration of the clin. complications in diabetes.

REFERENCE COUNT: 107 THERE ARE 107 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:241373 CAPLUS

DOCUMENT NUMBER: 129:49004

TITLE: Potential therapeutic value of drugs inhibiting semicarbazide-sensitive amine oxidase: vascular cytoprotection in diabetes mellitus

AUTHOR(S): Ekblom, Jonas

CORPORATE SOURCE: Department of Medical Pharmacology, Uppsala University, Uppsala, S-751 24, Swed.

SOURCE: Pharmacological Research (1998), 37(2), 87-92

CODEN: PHMREP; ISSN: 1043-6618

PUBLISHER: Academic Press Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 68 refs. Semicarbazide-sensitive amine oxidase (SSAO) is a copper-containing enzyme found in large amts. in blood plasma and in vascular smooth muscle. The catalytic activity of this enzyme is elevated in diabetes mellitus and some substrates, such as aminoacetone and methylamine also occur in increased amts. in this disease. After deamination by SSAO highly angiotoxic products are formed, methylglyoxal and formaldehyde, resp. Moreover, hydrogen peroxide is also formed as a side-product. These products arising from SSAO-catalyzed reactions may partially explain late-diabetic damages in the kidneys, eyes and peripheral nerves, as well as other cardiovascular disorders. It is therefore proposed that inhibition of SSAO may decrease the formation of these cytotoxic products and therefore prevent or slow the development of late-diabetic complications.

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:213800 CAPLUS

DOCUMENT NUMBER: 124:253988

TITLE: Mammalian plasma and tissue-bound semicarbazide-sensitive amine oxidases: biochemical, pharmacological and toxicological aspects

AUTHOR(S): Lyles, G. A.

CORPORATE SOURCE: Dep. Pharmacol. Clinical Pharmacol., Univ. Dundee, Dundee, DD1 9SY, UK

SOURCE: International Journal of Biochemistry & Cell Biology (1996), 28(3), 259-74

CODEN: IJBBFU; ISSN: 1357-2725

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with .apprx.140 refs. Mammalian plasma and tissues contain various soluble and membrane-bound enzymes which metabolize the synthetic

amine benzylamine particularly well. The sensitivity of these enzymes to inhibition by semicarbazide and related compds. suggests that they contain a cofactor with a reactive carbonyl group, which has been proposed to be either pyridoxal phosphate, pyrroloquinoline quinone or (more recently) 6-hydroxydopa. It is not yet clear if all of these semicarbazide-sensitive amine oxidases (SSAOs) are copper-dependent enzymes. A variety of compds. have now been identified as relatively selective inhibitors to distinguish the SSAOs from other amine oxidases, to investigate the properties of SSAOs and their potential role in biogenic and xenobiotic amine metabolism in vivo. While plasma SSAO is soluble, most tissue SSAOs appear to be membrane-bound, probable plasmalemmal enzymes, which may be capable of metabolizing extracellular amines. Vascular (and non-vascular) smooth muscle cells have particularly high SSAO activity, although recently the enzyme has been found in other cell types (e.g. adipocytes, chondrocytes, odontoblasts) implying a functional importance not restricted solely to smooth muscle. The substrate specificity of plasma and tissue SSAOs shows considerable species-related variations. For example, while some endogenously-occurring aromatic amines such as tyramine and tryptamine are metabolized well by SSAO in homogenates of rat blood vessels, and also in vitro inhibition of SSAO can potentiate vasoconstrictor actions of these amines in rat vascular preps., these amines are poor substrates for human SSAO, thus complicating attempts to generalize possible physiol. roles for these enzymes. Vascular SSAO can metabolize the xenobiotic amine, allylamine administration to produce cardiovascular lesions in exptl. animals, sometimes mimicking features of atherosclerotic disease. Recent studies showing that the endogenously-occurring aliphatic amines methylamine and aminoacetone are metabolized in vitro to formaldehyde and methylglyoxal, resp., by SSAO in some animal (including human) tissues, suggest the possibility that toxicol. consequences upon cellular function could result if such conversions occur in vivo.

L34 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:95966 CAPLUS

DOCUMENT NUMBER: 124:139297

TITLE: Semicarbazide-sensitive
amine oxidases: some biochemical
properties and general considerations

AUTHOR(S): Buffoni, F.

CORPORATE SOURCE: Dep. of Preclinical and Clinical Pharmacology, Univ.
of Florence, Italy

SOURCE: Progress in Brain Research (1995),
106 (Current Neurochemical and Pharmacological Aspects
of Biogenic Amines), 323-31
CODEN: PBRR44; ISSN: 0079-6123

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review, with 74 refs. Semicarbazide-sensitive amine oxidases with a high affinity from benzylamine (Bz.SSAO) (E.E.1.4.3.6) have been biochem. described in many mammalian tissues (adipose tissue, lung, heart, blood vessels). The enzymic activity appears to be expressed by mesenchymal cells (fibroblasts, adipocytes, smooth muscles). Although the physiol. role of this enzymic activity is still unclear, some possible physiol. substrates such as histamine are discussed. Some enzymes of this class (SSAO) have been purified. They share many similarities, among which are that they contain copper and a carbonyl active site. The nature of the organic cofactor of these enzymes is discussed and data are presented which have identified pyridoxal in pig kidney diamine oxidase and in pig plasma

benzylamine oxidase by gas chromatog.-mass spectrometry.

L34 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:95964 CAPLUS

DOCUMENT NUMBER: 124:139296

TITLE: Substrate-specificity of mammalian
tissue-bound semicarbazide-sensitive
amine oxidase

AUTHOR(S): Lyles, G. A.

CORPORATE SOURCE: Dep. of Pharmacology and Clinical Pharmacology, Univ.
of Dundee, Dundee, DD1 9SY, UK

SOURCE: Progress in Brain Research (1995),
106(Current Neurochemical and Pharmacological Aspects
of Biogenic Amines), 293-303
CODEN: PBRRA4; ISSN: 0079-6123

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review, with 94 refs. Although the existence of a membrane-bound (probably plasmalemmal) semicarbazide-sensitive amide oxidase (SSAO) is well established in various mammalian tissues, and especially within vascular smooth muscle, its importance and the possible consequences of its metabolism of certain physiol. and xenobiotic amines in vivo are under continuing investigation. In this respect, there are major species-related differences in substrate specificity determined in vitro, not only towards the synthetic amine benzylamine, but also towards some other aromatic amines (e.g. tyramine, tryptamine, 2-phenylethylamine, dopamine, histamine) which are possible endogenous substrates. Inhibition of SSAO can potentiate the pharmacol. activity of some amines in isolated tissue (e.g. blood vessel) preps. from some species. Recent evidence has accumulated that SSAO may also be involved in metabolizing endogenous aliphatic amines such as methylamine and aminoacetone, focusing attention on the fact that the aldehyde products (formaldehyde and methylglyoxal, resp.) are potentially cytotoxic agents. Indeed, SSAO has been implicated in exptl. models of cardiovascular toxicity involving conversion of the industrial aliphatic amines allylamine to acrolein. In summary, metabolism by SSAO may reduce the physiol./pharmacol. effects of some amines, but the resulting metabolites (aldehydes, H₂O₂) may also have important actions.

L34 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:991359 CAPLUS

DOCUMENT NUMBER: 124:75802

TITLE: Further studies on the ex vivo effects of procarbazine
and monomethylhydrazine on rat semicarbazide
-sensitive amine oxidase
and monoamine oxidase activities.

AUTHOR(S): Holt, Andrew; Callingham, Brian A.

CORPORATE SOURCE: Dep. Pharmacol., Univ. Cambridge, Cambridge, CB2 1QJ,
UK

SOURCE: Journal of Pharmacy and Pharmacology (1995),
47(10), 837-45

CODEN: JPPMAB; ISSN: 0022-3573

PUBLISHER: Royal Pharmaceutical Society of Great Britain

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Following administration of procarbazine, or one of its metabolites, monomethylhydrazine, to rats, activities of monoamine oxidases A and B (MAO A and MAO B) and of semicarbazide-sensitive amine oxidase (SSAO) were measured ex-vivo. Both compds. were potent inhibitors of SSAO in tissue homogenates, exhibiting ID₅₀ values in most tissues of approx. 8 mg kg⁻¹

(procarbazine) and 0.08 mg kg⁻¹ (monomethylhydrazine). Concurrent dose-dependent inhibition of MAO activities did not occur. In the liver, potentiation of MAO B activity, to 140% of that in controls, was apparent following monomethylhydrazine, and this effect was independent of the drug dose. Both compds. produced a dose-dependent potentiation of MAO A in brown adipose tissue, the elevation being more pronounced following monomethylhydrazine, with activity rising to 350% of that in control homogenates. In a parallel in vitro study, monomethylhydrazine was without effect on MAO A in brown adipose tissue homogenates. By perfusing the SSAO substrate, benzylamine, through the isolated mesenteric arterial bed of the rat, it was found that pretreatment of animals with procarbazine or monomethylhydrazine reduced metabolism of this amine by a similar degree as had been determined ex-vivo in blood vessel homogenates. Thus, these compds. would be suitable for use as selective inhibitors in pharmacol. exams. of SSAO function in isolated tissues and organs.

L34 ANSWER 24 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:373361 CAPLUS
DOCUMENT NUMBER: 122:122481
TITLE: Aminoacetone metabolism by semicarbazide-sensitive amine oxidase in rat aorta
AUTHOR(S): Lyles, Geoffrey A.; Chalmers, Janette
CORPORATE SOURCE: Dep. Pharm. Clin. Pharm., Univ. Dundee, Dundee, DD1 9SY, UK
SOURCE: Biochemical Pharmacology (1995), 49(3), 416-19
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB High speed (105,000 g/60 min) membrane fractions from rat aorta homogenates metabolized the aliphatic amine aminoacetone (AA) to methylglyoxal (MG) with a Km of $19 \pm 3 \mu\text{M}$, and Vmax of 510 ± 169 nmol MG/h/mg protein. This deaminating activity appears to be due to a semicarbazide-sensitive amine oxidase (SSAO), which is associated with smooth muscle cells in blood vessels of the rat and other species. AA was a competitive inhibitor (K_i of $28 \pm 6 \mu\text{M}$) of the metabolism of benzylamine, a synthetic amine often used as an assay substrate for SSAO. AA is produced endogenously from mitochondrial metabolism of threonine and glycine, and thus could be a physiol. substrate for SSAO, whereas the production of MG by SSAO could have cytotoxic implications for cellular function.

L34 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:213325 CAPLUS
DOCUMENT NUMBER: 120:213325
TITLE: Semicarbazide-sensitive amine oxidase and monoamine oxidase in rat brain microvessels, meninges, retina and eye sclera
AUTHOR(S): Zuo, Dong Mei; Yu, Peter H.
CORPORATE SOURCE: Dep. Psychiatry, Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.
SOURCE: Brain Research Bulletin (1994), 33(3), 307-11
CODEN: BRBUDU; ISSN: 0361-9230
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Monoamine oxidase-A and -B (MAO-A and MAO-B) and semicarbazide-sensitive amine oxidase (SSAO) activities were assessed in several rat micro-vascular

tissues and eyes using selective substrates and inhibitors. In rat brain microvessels both MAO-A and MAO-B activities are relatively high and the levels of the two types of MAO's are comparable. Retina possesses a similar ratio of MAO-A and B but the activities are much lower. Eye sclera and meninges exhibit mainly MAO-A and MAO-B, resp. Aorta is the only tissue where SSAO is the predominant amine oxidase. Relatively low, but significant amts. of SSAO were also detected in brain microvessels, meninges, retina and eye sclera. Methylamine was observed to be deaminated by SSAO from different tissues. The physiol. and toxicol. implications of amine oxidases in these tissues are discussed.

L34 ANSWER 26 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:211661 CAPLUS

DOCUMENT NUMBER: 116:211661

TITLE: The metabolism of aminoacetone to methylglyoxal by semicarbazide-sensitive amine oxidase in human umbilical artery

AUTHOR(S): Lyles, Geoffrey A.; Chalmers, Janette

CORPORATE SOURCE: Dep. Pharmacol., Ninewells Hosp., Dundee, DD1 9SY, UK

SOURCE: Biochemical Pharmacology (1992), 43(7); 1409-14

CODEN: BCPCA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aliphatic amine aminoacetone has been described previously as a product of mitochondrial metabolism of threonine and glycine. Here, aminoacetone is shown to be deaminated to methylglyoxal by supernatants obtained by low speed centrifugation (600 g/10 min) of human umbilical artery homogenates, and also by membrane fractions isolated by high speed centrifugation (105,000 g/60 min) of these supernatants. Metabolism of 100 μ M aminoacetone was completely inhibited by 1 mM propargylamine and MDL 72145, drugs which are capable of inhibiting the membrane-bound semicarbazide-sensitive amine oxidase (SSAO) activity found in vascular smooth muscle cells, whereas 1 mM pargyline and deprenyl which are inhibitors of monoamine oxidase, were without inhibitory effect. Estimated kinetic consts. (at pH 7.8) for aminoacetone metabolism were $K_m = 92 \mu$ M; $V_{max} = 270 \text{ nmol/h/mg protein}$. In addition, aminoacetone was a competitive inhibitor ($K_i = 83 \mu$ M and 128 μ M in low speed supernatants and high speed membrane fractions, resp.) of [^{14}C]benzylamine metabolism by SSAO in this tissue. Aminoacetone would appear to be an endogenously occurring amine with a K_m for metabolism by SSAO far lower than other aliphatic and aromatic biogenic amines examined previously as potential physiol.

substrates for the human vascular enzyme and possible implications of this are discussed.

L34 ANSWER 27 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1989:624777 CAPLUS

DOCUMENT NUMBER: 111:224777

TITLE: The influence of amine-metabolizing enzymes on the pharmacology of tyramine in the isolated perfused mesenteric arterial bed of the rat
AUTHOR(S): Elliott, Jonathan; Callingham, Brian A.; Sharman, Dennis F.

CORPORATE SOURCE: Dep. Pharmacol., Univ. Cambridge, Cambridge, CB2 1QJ, UK

SOURCE: British Journal of Pharmacology (1989), 98(2), 515-22

CODEN: BJPCBM; ISSN: 0007-1188

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The pressor response to the infusion of tyramine (Tyr) into the isolated perfused mesenteric arterial bed of the rat was studied at both a low and a high dose (0.2 and 2.0 μmol) and the effect of monoamine oxidase-A (MAO-A) and semicarbazide-sensitive amine oxidase (SSAO) inhibition was examined. Very little MAO-B activity is found in homogenates of this tissue when Tyr is used as substrate. Inhibition of SSAO by treating rats with MDL 72145 1 h before dissection had no effect on the maximum pressure attained or the area under the curve (AUC) of the response to both low and high doses of Tyr. Inhibition of MAO-A, by inclusion of 10 μM clorgyline in the perfusing fluid, resulted in no potentiation at both low or high doses of Tyr. The inhibition of both these enzymes together substantially increased the AUC of the pressor response. Cocaine (3 μM) potentiated the responses to adrenaline (Ad). At this dose, cocaine reduced the peak height and the AUC of the responses to both doses of Tyr. Inhibition of extraneuronal uptake mechanisms with corticosterone (29 μM) did not potentiate the response to Ad and did not alter the response to Tyr (low dose). The effects of MDL 72145 and clorgyline on the directly acting amine Ad were studied. MDL 72145 caused a small increase in the EC_{50} and in the maximum response to Ad, while clorgyline (10 μM) increased the EC_{50} value slightly and decreased the maximum response. When the 2 inhibitors were used in combination, a significant increase in the maximum response (but no change in the EC_{50}) was seen. These data indicate that the action of Tyr in this vascular bed is, at least partly, indirect. Inactivation of Tyr is affected by both MAO-A and SSAO in the blood vessel wall. Inhibition of both enzymes seems to be necessary to achieve potentiation of the pressor response. The effects of these enzyme inhibitors on directly acting amines may mask any potentiation of the response when MAO-A or SSAO alone is inhibited.

L34 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1988:625485 CAPLUS

DOCUMENT NUMBER: 109:225485

TITLE: Properties of a semicarbazide-sensitive amine oxidase in human umbilical artery

AUTHOR(S): Precious, Elaine; Lyles, Geoffrey A.

CORPORATE SOURCE: Dep. Pharmacol. Clin. Pharmacol., Univ. Dundee, Dundee, DD1 9SY, UK

SOURCE: Journal of Pharmacy and Pharmacology (1988), 40(9), 627-33

CODEN: JPPMAB; ISSN: 0022-3573

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The metabolism of some aromatic amines by amine oxidase activities in human umbilical artery homogenates was studied. The inhibitory effects of clorgyline showed that 5-hydroxytryptamine (5-HT) and tryptamine, 1 mM, were predominantly substrates for monoamine oxidase (MAO) type A, whereas MAO-A and B were both involved in the metabolism of β -phenylethylamine (PEA), 100 μM , and tyramine, 1 mM. About 20-30% of tyramine and PEA metabolism was resistant to 1 mM clorgyline, but sensitive to inhibition by semicarbazide, 1 mM, indicating the presence of a semicarbazide-sensitive amine oxidase (SSAO). Benzylamine, 1 mM, appeared to be metabolized exclusively by SSAO with a K_m (161 μM) at pH 7.8 similar to that found for SSAO in other human tissues. Tyramine and PEA were relatively poor substrates for SSAO, with very high apparent K_m values of 17.6 and 13.3 mM, resp., when determined in the presence of clorgyline, 10-3M, added to inhibit any metabolism of those amines by MAO activities. However, kinetic studies with benzylamine indicated that clorgyline, 10-3M, also appears to inhibit SSAO competitively such that the true K_m values for tyramine and PEA

may be .apprx.60% of those apparent values given above. No evidence for the metabolism of 5-HT or tryptamine by SSAO was obtained. The aliphatic amine methylamine was recently shown to be a specific substrate for SSAO in umbilical artery homogenates. Benzylamine and methylamine were used as SSAO substrates in histochem. studies to localize SSAO in tissue sections. Both amines promoted tissue staining which occurred predominantly over the medial layers of the vessel wall, and this staining was prevented by the presence of semicarbazide, 1 mM, but not by pargyline, 1 mM, in the reaction medium. The results support the notion that smooth muscle cells are an important site of SSAO activity in human blood vessels and reinforce the possibility that methylamine, an endogenously occurring amine, may be a better candidate as a physiol. substrate for SSAO in man than several aromatic biogenic amines so far examined

L34 ANSWER 29 OF 29 USPATFULL on STN

ACCESSION NUMBER: 2001:136427 USPATFULL
 TITLE: Synthetic polynucleotides
 INVENTOR(S): Weiss, Anthony Steven, Sydney, Australia
 PATENT ASSIGNEE(S): The University of Sydney, Sydney, Australia (non-U.S. corporation)

| | NUMBER | KIND | DATE | |
|---------------------|----------------|------|----------|-----------------|
| PATENT INFORMATION: | US 6277622 | B1 | 20010821 | <-- |
| | WO 9806830 | | 19980219 | <-- |
| APPLICATION INFO.: | US 1999-242095 | | 19990208 | (9) |
| | WO 1997-AU505 | | 19970811 | |
| | | | 19990208 | PCT 371 date |
| | | | 19990208 | PCT 102(e) date |

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 LEGAL REPRESENTATIVE: Howson and Howson
 NUMBER OF CLAIMS: 7
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 12 Drawing Figure(s); 12 Drawing Page(s)
 LINE COUNT: 1967

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to synthetic polynucleotides which encode lysyl oxidase, lysyl oxidase like molecules or variants of these species. The synthetic polynucleotides of the invention permit the expression of functional lysyl oxidase, lysyl oxidase like molecules or variants of these species, typically in good yield. The invention also relates to recombinant DNA molecules containing these, synthetic polynucleotides, to cells containing them and to uses of the expression products.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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